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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,287	05/10/2001	Robert Klein	R00208US (#9	1252

7590 02/23/2004

D Peter Hochberg Company
6th Floor
1940 East 6th Street
Cleveland, OH 44114-2294

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,287	KLEIN ET AL.	
	Examin r	Art Unit	
	Isis Ghali	1615	

-- Th MAILING DATE of this communication appears on the cover sh t with th correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *17 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 11-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9 and 11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment, filed 11/17/2003.

Claims 1, 3-9, 11-18 are included in the prosecution.

The following new ground of rejection is necessitated by applicant's amendment:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-, 3-9, 11-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not disclose anywhere that the polyacrylate not comprising amino group, and this introduces a new matter.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3-9, 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are confusing as they recite the supersaturated reservoir because in order to have a supersaturated reservoir, there should be a solvent that dissolves the active agents till it reaches saturation, and then rendered supersaturated by other elements such as heat or adding crystallization inhibitor. Clarification is requested.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3-9 and 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,730,999 ('999) in view of any of US 5,683,711 ('711) or WO 97/23227 ('227).

Claim 1 reads as a transdermal therapeutic system comprising backing layer, a protective release liner, and a reservoir comprising polyacrylate adhesive not containing amino group, amino group containing polymer and combination of estradiol and norethisterone in a supersaturated state. The amino-group containingg polymer is selected from polyaminoamides, polyaminoimidazolines, polyurethaneamines, polyamines and polyglucosamines.

US '999 teaches a dermal therapeutic system which exhibits prolonged release of the drug comprising at least one pharmaceutical agent combined with poly(meth)acrylates in the form of at least one layer of the therapeutic system. The poly(meth)acrylates are mixture of at least one (meth)acrylic polymer containing functional groups and at least one (meth)acrylic polymer which contains no functional group or only insignificant amount of functional groups (abstract; col.2, lines 66-67; col.3, lines 1-7). The ratio of the functional and non-functional polymers depends on the release properties of the pharmaceutical agent and the flow behavior of the product blend (col.3, lines 9-14). The reference disclosed a method of preparing the dermal therapeutic system including stirring the drug and the polymers (col.5, lines 31-39, 55-

61). The drugs included hormones (col.5, line 3). Examples of amino-containing polymer is methacrylamide (col.3, lines 47-53).

US '999 does not disclose the mixture of the hormones in the supersaturated state or the specific species of the amino containing polymer.

It is within the skill in the art to replace one species by another when both are know to perform the same function. The claimed species of the amino-containing polymers do not impart patentability to the claims, absent evidence to the contrary.

US '711 teaches a transdermal patch comprising estradiol and norethisterone in a supersaturated state in acryl ate adhesive matrix and the viscosity of the adhesive matrix can inhibit crystallization of the supersaturated adhesive (col.6, lines 31-35, 61-62; col.8, lines 41-47; col.9, lines 23-25; col.10, lines 52-58). The reference teaches that the supersaturation is desirable and necessary in order to impart a high thermodynamic activity to drugs which permeate with difficulty (col.6, lines 40-45). The amount of estradiol/NETA is 2.5%/10% (col.10, Table 3).

WO '227 teaches a transdermal patch for release of estradiol and progesterone comprises a backing layer; a protective release liner; and an active ingredient pressure sensitive adhesive matrix layer containing combination of estradiol and norethisterone acetate and crystallization inhibitor (abstract; page 4, first and forth paragraphs; page 7, first full paragraph). The pressure sensitive adhesive matrix layer is acrylate copolymers (page 5, last paragraph). The matrix includes estradiol and norethisterone (NETA) in a supersarurated state. The estradiol is between 0.6 to 1.8 % and the NETA is between 4.0 to 10.0 % (page 6, last paragraph). The pressure sensitive adhesive is solvent

based (Example 1, page 8). The reference teaches that the transdermal patch comprising estradiol and NETA in supersaturated state in the copolymeric matrix is the condition which confers to the active ingredients activity required for a forced diffusion through the skin even in absence of absorption enhancer, and could release constant amounts of the drugs during its whole possible application time from 3-7 days (page 4, last paragraph; page 6, last paragraph).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device comprising a reservoir of acrylate adhesive comprising hormones and mixture of polymer having no amino group and amino group containing polymer as disclosed by US '999, and replace the hormones by supersaturated state of the hormones as disclosed by any of US 711 and WO '227, motivated by the teaching of US '711 that the supersaturation is desirable and necessary in order to impart a high thermodynamic activity to drugs which permeate with difficulty, or motivated by the teachings of WO '227 that the transdermal patch comprising estradiol and NETA in supersaturated state in the copolymeric matrix is the condition which confers to the active ingredients activity required for a forced diffusion through the skin even in absence of absorption enhancer, and could release constant amounts of the drugs during its whole possible application time from 3-7 days, with reasonable expectation of having a transdermal delivery device comprising a combination of estradiol and NETA in a supersaturated state in a mixture of amino-containing polymer and amino-free polymer without crystallization that deliver the combination of the hormones to the patient in need with great success.

Response to Arguments

8. Applicant's arguments with respect to claims 1, 3-9 and 11-18 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595.

The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)305-1235.

Isis Ghali
Examiner
Art Unit 1615

Gollamudi S. Kishore, PhD
Primary Examiner
Group 1500